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EDITORIAL COMMENT

The Rise and Fall of Aspiration Thrombectomy*

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The hallmark of ST-segment elevation myocardial infarction (STEMI) is thrombotic occlusion of an epicardial vessel. As many as 50% of patients undergoing primary percutaneous coronary intervention (PCI) demonstrate distal embolization and microvascular obstruction despite achieving normalized epicardial flow. This is associated with increased infarct size, reduced recovery of ventricular function, and reduced survival (1,2). In an effort to reduce distal embolization, a number of thrombectomy devices have been studied for use with primary PCI. The story of aspiration thrombectomy is a sterling example of the utility of evidence-based medicine in contemporary clinical practice, where initial exuberance for a new therapy was tempered by a more limited or measured application on the basis of accrual of high-quality data. Some of the salient features are discussed in the following text.

THE RISE

TAPAS (Thrombus Aspiration during Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) was one of the sentinel trials in this field (n = 1,071). At 1 year, there were significant reductions in all-cause (4.7% vs. 7.6%; p = 0.04) and cardiovascular (3.6% vs. 6.7%; p = 0.02) mortality, with a trend toward reduction in subacute and late stent thrombosis with adjunctive aspiration thrombectomy compared with conventional PCI alone (3). Although the trial was criticized for its limitations (possible selection bias [single-center study], unclear mechanism [no difference in enzymatic infarct size post-procedure but a significant difference in cardiovascular and all-cause mortality at 1 year], and possibility of chance [trial was not powered for mortality]), the overall clinical outcomes were directionally consistent with other smaller trials (2). On the basis of this data, aspiration thrombectomy received a Class IIa recommendation for use with PCI in the 2009 American College of Cardiology (ACC)/ American Heart Association (AHA) STEMI guidelines (4).

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Commensurate with the timeframe of evidence accrual, there appeared to be a gradual uptake of aspiration thrombectomy in clinical practice the world over. In this issue of *JACC: Cardiovascular Interventions*, Sirker et al. (5) estimate that the uptake of adjunctive thrombectomy in the United Kingdom was around 50% by 2010 to 2011.

THE FALL

The INFUSE-AMI (Infuse-Acute Myocardial Infarction) trial failed to replicate the findings of the TAPAS trial in 452 patients, with no differences observed in infarct size with aspiration thrombectomy at 30 days (6). Despite this, on systematic review, the totality of evidence still favored a benefit in clinical outcomes with aspiration thrombectomy, particularly on longer-term follow-up (7), and it remained a Class IIa recommendation in the 2013 ACC/AHA STEMI guidelines (8).

TASTE (Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia) was a large, multicenter, registry-based randomized clinical trial (n = 7,244). There were no differences in clinical

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outcomes assessed at 1 year between aspiration thrombectomy versus conventional PCI, including all-cause mortality (5.3% vs. 5.6%; p = 0.57) or stent thrombosis (0.7% vs. 0.9%; p = 0.51) (9). TOTAL (Trial of Routine Aspiration Thrombectomy with PCI versus PCI Alone in Patients with STEMI) is the largest and most definitive trial on this topic to date (n = 10,732). No differences in clinical outcomes were observed at 6 months in favor of aspiration thrombectomy, including in the primary outcome of major adverse cardiovascular events (6.9% vs. 7.0%; p = 0.86), cardiovascular death (3.1% vs. 3.5%; p = 0.34), or stent thrombosis (1.5% vs. 1.7%; p = 0.42); stroke rates were higher with aspiration thrombectomy (0.7% vs. 0.3%; p = 0.02) (10). On the basis of this evidence, routine aspiration thrombectomy has been downgraded to a Class III recommendation in the most recent (2015) iteration of the ACC/AHA STEMI guidelines (11).

The current study by Sirker et al. (5) provides further evidence against routine aspiration thrombectomy use during primary PCI. They included 98,176 STEMI patients undergoing primary PCI from the U.K. national PCI registry. On propensity analysis, there was no difference in 1-year mortality between any form of thrombectomy versus conventional PCI, including adjunctive aspiration thrombectomy and conventional PCI (n = 85,675; p = 0.96) (5). This is an important body of work on a large cohort of patients. However, causative inferences regarding therapeutic choices from observational datasets can be hard at best, and outright wrong at worst, as unmeasured confounders can obfuscate all and any statistical adjustments. Physicians frequently make therapeutic decisions on the basis of characteristics that can be hard to capture in registries (such as frailty, "eyeball test," and so on). In such settings, inverse probability of treatment weights may be a less confounded way of performing a propensity analysis, wherein individuals are weighted by the inverse probability of receiving the treatment that they actually received. In the current study, the authors chose to perform a more conventional propensity analysis, thus being potentially more vulnerable to selection biases. However, the results of the current study are directionally consistent with recent randomized controlled trials, and are thus less likely to be spurious. Coding errors may also be present in registries. For example, patients in this study that did not receive thrombectomy were older, more frequently had diabetes, less frequently smoked, and more frequently had preprocedure Thrombolysis In Myocardial Infarction 2 to 3 flow. Although these patients were classified as "STEMI," such characteristics more closely resemble that of non-STEMI, which carries a different prognosis than STEMI. Left ventricular ejection fraction was also missing for a large proportion of patients, which is an important determinant of outcomes following STEMI, and may also result in unmeasured confounding. However, the authors performed sensitivity analyses using both nonimputed and imputed data for LVEF and report a similar treatment effect (5).

In summary, routine aspiration thrombectomy was once considered a relatively simple technique to improve long-term outcomes in the care of STEMI patients. Thrombus removal remains an intuitively valid concept; however, thrombus removal is more complex than initially appreciated. Future studies will need to similarly rigorously evaluate the role of selective thrombectomy versus no thrombectomy, determine more effective thrombectomy devices, and better discriminate appropriate lesions to which this therapy can be applied.

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